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Ocular surface changes induced by silicone-hydrogel contact lenses

Thesis for the scientific title of Doctor in Medicine

Summary

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SIBIU 2013

Contact lenses have been developed for more than a hundred years and progresses in Contactology are spectacular. The evolution of knowledge in corneal and ocular surface physiology led in parallel to considerable progress concerning contact lenses, allowing distribution of this type of optical correction and therapy in a large population and of all ages.

Emergence of soft contact lenses in the 70s, was one of the most significant discoveries of the last century, a vast area that currently includes more than 140 million wearers worldwide.

In the early 80's researchers began using thinner materials to manufacture lenses with a high water content, increasing oxygen transmissibility and permeability level in order to improve the physiological response of the cornea. Also at that time it was established the demand of oxygen at the corneal level and the minimum oxygen level that a contact lens must provide while wearing during day or night in order to eliminate the corneal edema.

After all this it took another decade for the industry and staff to develop the first soft contact lens with high oxygen permeability. This achievement was almost magical because researchers have struggled for years to find a way to incorporate in silicone elastomer in the hydrogel polymer.

The first report on the physiological benefits of the silicone-hydrogel contact lenses was presented in 1995 at ARVO meeting - Association for Research and Vision in Ophthalmology and after another 3 years the first silicone-hydrogel lenses appeared.

Fitting of contact lenses and education of wearers cannot be achieved only with medical knowledge because it is also necessary a careful selection of wearers, followed by appropriate recommendations on the type of contact lens, multipurpose solutions, how to wear and replacement and also prevention and early detection of possible complications.

Eye care practitioners are responsible for recommending contact lenses taking into account all the factors involved, try to develop with caution the indications for optical correction and therapeutic with soft contact lenses, especially silicone-hydrogel and to critically evaluate clinical their performance in order to validate their usefulness for the benefit of the wearer.

Numerous studies have been conducted to date to determine the effect of contact lenses on the cornea and anterior segment. Because of the potential risk of serious

complications leading to blindness, researches have focused on corneal infections, particularly related to the extended port, which were associated with a greater risk for microbial keratitis. Daytime wearing remains the main way of wearing contact lenses hydrogel and silicone-hydrogel even with high permeability for oxygen, even if the last ones were originally introduced for extended port.

Although corneal injury other than microbial keratitis, is not threatening to vision loss, such situations can cause the wearer discomfort and discontent, which eventually lead to abandonment behavior. Silicone-hydrogel lenses were associated with superior epithelial arcuate lesions (SEALs), papillary conjunctivitis induced by contact lenses CLPC, and other mechanical complications.

Recently, Jones et al questioned corneal staining resulting from silicone-hydrogel contact lenses used in combination with various multipurpose solutions and suggested an association between this phenomenon and the corneal inflammation and the reduction in comfort during wear.

Success in adapting lenses nowadays is often judged by the patient point of view and his degree of adaptation rather than by obtaining satisfactory performance based on specific criteria, especially since ophthalmologists now have lenses made of sophisticated materials, with improved design for the correction of all refractive errors.

Since 1971, there were attempts to define standards for successful wearing contact lenses in PMMA, which included criteria such as wearing period, comfort, vision, corneal changes and the appearance of the wearer.

During this study I intend to analyze how silicone-hydrogel contact lenses interact with ocular surface and to highlight the changes occurring during wearing period in relation to different types of lenses used, multipurpose solutions and the replacement and wearing modality.

Also I wanted to elaborate a set of evaluation criteria for silicone-hydrogel contact lens wearing and wearers and to compare the performance of different lenses available and I tried to review the successful standards known so far and to draw several criteria for prescribers to compare clinical performance of silicone-hydrogel contact lenses used in daily wear and extended wear.

This paper is based on a prospective, observational study conducted in Emergency Clinical Hospital of Sibiu - Ocular Surface Research Center and the optical shop OFTA CENTER Brasov, during September 2011 - October 2012.

Of all patients that were presented in both ophthalmology services during that period we selected a total of 86 patients fitted with silicone-hydrogel lenses. All selected patients were informed about the inclusion in the study and it was explained the noninvasive nature of the methods used and obtained their consent to participate according to the Declaration of Helsinki on human subjects studies.

Study inclusion criteria were as follows:

• Over 18 years because all participants signed an informed consent that have agreed to participate in the study and comply with the study protocol

• Contact lens wearers at the start of the study, but with a break of wearing at least 2 weeks before study

• Absence of ocular or systemic signs that contraindicate contact lens wear

Exclusion criteria were - patients with:

• Active corneal infection or inflammation

• Acute or sub acute inflammation or infection of the anterior chamber

• Any injury or eye disease

• Any disorder of the cornea, conjunctiva or eyelids that could affect contact lens wear

• Systemic disease or use of medications that could affect the ocular surface

• Pregnancy

• Operated with refractive surgery

• Objective ophthalmologic examination was always preceded by a targeted history of the patient in order to obtain information about its particularities in relation to contact lenses: determine possible contraindications, analysis of risks versus benefits and review of measures concerning applying / removing the lens, their care and period of wear and replacement.

• All patients completed at the beginning and end of the study a questionnaire to assess the knowledge and habits of wearing contact lenses and their care and the degree of satisfaction related to performance of lens wear.

Contact lens wearers assessment questionnaire included 21 questions and was conducted in collaboration with Ocular Surface Research Center in Sibiu and was composed of three parts: the first part - the first 6 questions were used to identify study participants and history characteristic of contact lenses (including assessing their knowledge about the type of lenses and solution used), the second part of the questionnaire - following 9 questions intended to assess subjective experience of contact lens wearer (comfort, vision, dry eye symptoms , eye redness), and the last part of the questionnaire - 5 questions evaluated the extended wear related to comfort in contact lenses.

Initial examination protocol included: refraction, keratometry, visual acuity with and without correction, contact lens slit lamp examination, tear film, eyelids and eyelashes, conjunctiva, cornea and limbus. Visual acuity depends largely on the quality of the tear film.

Ophthalmological examination stages:

• Determining visual acuity with and without correction using Snellen optotype, determining refractive errors.

• Keratometry was performed autorefractometer MRK-3100P Huvitz

• Pachymetry was done with Visante OCT 3.0 from Carl Zeiss, optical coherence tomography for evaluation of anterior segment

• Assessing adaptation of contact lenses and anterior segment biomicroscopy was performed with slit lamp Topcon SL-D2 with camera attached DC-1. We analyzed the appearance of the eyelids, the conjunctiva, cornea and anterior chamber. To assess changes in the ocular surface in relation to contact lenses we used CCLRU scale.

• Evaluating of NITBUT, Non-invasive tear film break-up time was achieved with Keratograph V from Oculus; the Keratograph was focused on each eye, the patient was asked to blink and then try to stop blinking a time. The software recorded the time to onset and the time when appeared the first distortion. I considered NITBUT value as the average of three consecutive measurements.

Any changes of the ocular surface, including the variation of track parameters as CCLRU assessment scale was recorded and staged for inclusion in the study.

Silicon - Hydrogel contact lenses used were those available at the moment in Romania, for daily wear up to 14 or 30 days and extended (7 days) or continuous (30 days):

• Lotrafilcon A - to wear up to 30 days, BC 8.4 and 8.6 mm, 13.8 mm diameter.

• Balafilcon A - to wear up to 30 days, BC 8.6 mm, diameter 14 mm.

• Senofilcon A - to wear up to 14 days, BC 8.4, diameter 14 mm.

In the first part of the study we analyzed the questionnaire responses of the 86 patients wearing silicone-hydrogel contact lenses.

To analyze the association between different pairs of variables we used nonparametric Spearman correlation. P-value <0.05 indicates a statistically significant association. Descriptive statistics (mean, standard deviation / median, interquartile range) was used to present the demographic characteristics of the study group and presenting results: keratometry, pachymetry, NIBUT and the fluorescein corneal staining.

In the second part we analyzed and presented the incidence of ocular surface changes which have occurred during the study and reviewed responses to the questionnaire on comfort and vision.

Patients were aged between 18 and 56 years. The average age of patients was 33.4 ± 11.9 years. Of the 86 patients enrolled, 75 were women, representing 87% of the total, and most wore contact lenses for several years, the average behavior of at least 5 years for more than 50% of participants.

In the study, subjective comfort was evaluated at the end of the study, through a series of questions that focused on global comfort with contact lenses, comfort at the end of the day, the quality of vision with contact lenses and vision at the end of the day. Most contact lens wearers use the lenses almost continuously for more than 5 days per week in 63% of cases, and subjective overall comfort and vision with contact lenses measured at the end of the wearing period of time were very good or excellent.

Comparing men and women I did not find a statistically significant difference, on the one hand related to comfort, with $p = 0.97$ and related to vision with $p = 0.90$.

Overall subjective assessment of comfort was significantly better compared to that at the end of the day and that at the end of the wearing period of lenses. ($P < 0.01$)

Evaluation of vision with contact lenses was also significantly better overall and at the end of the day compared to that at the end of the wearing period.

To characterize any corneal morphological changes in the study we evaluated at 2 weeks, 1 month and 3 months the variations of pachymetry and keratometry by comparing them to the mean values at baseline; to examine the associations between different pairs of variables we used nonparametric correlation Spearman, p-value <0.05 indicating a statistically significant association. The values obtained show the keratometry stability during the 3 months of wearing silicone hydrogel lenses. At one month, I noticed a change from baseline of the keratometry average (7.68 to 7.73) statistically significant (p <0.05), but clinically insignificant since after 3 months the values returned within the baseline.

As in the literature, we found significant correlations between corneal thicknesses measured at the end of 3 months between the 3 groups of silicone-hydrogel contact lens users. Studies by Myrowitz E.H. on the relationship between long-term wearing of contact lenses and corneal thickness showed that rigid contact lens wear is associated with a reduction in mean central corneal thickness but in soft contact lens wearers there was no significant variation corneal thickness compared to a lot of non contact lens wearers.

In the questionnaire applied to the study participants, the subjective assessment show that only 16% of wearers do not have discomfort during wear and 78% of them have rare and rarely discomfort. Rate of secretion and tear film stability, especially related to the aqueous phase and tear film break-time TBUT are lower in contact lens wearers. Decreased tear film volume is involved in discomfort and intolerant behavior. Evaporation is influenced by lipid layer status. It has been showed that evaporation increases in contact lens wearers. Noninvasive break-up time of tear film NI-BUT can vary from very low time <10s to very good> 30s. Contact lens wearers complaining of discomfort during wear can have a NI-BUT from 3-10s, values similar to those seen in patients with moderate forms of kerato-conjunctivitis Sicca. In most studies, tear film break between 2-3 seconds on the surface of a rigid contact lenses and 5-6 seconds on the surface of soft contact lenses. Young and Efron showed that TBUT occurs at 3-10s at the surface of hydrogel lenses.

In our study we obtained an average value of 8.04s in silicone-hydrogel contact lens wearers for NI- BUT evaluated at the end of the study and we did not find a statistically significant change from baseline measurements.

Using CCLRU scale, we evaluated conjunctival hyperemia in both eyes at the end of the study, in the regions nasal, temporal, superior and inferior and I calculated the average score obtained for the global hyperemia of conjunctiva. Using the statistical analysis of the results for conjunctival hyperemia, we obtained a statistically significant change between baseline level and hyperemia assessed at one month of wear. ($P = 0.005$)

Although there were variations in the NI-BUT during the study, they were not statistically significant. NI- BUT value decreased by 0.92s and 1.6s at 2 weeks and one month after compared to baseline, but after two months this value increased back with 1.48s. After 3 months of use, the difference between initial and final mean value was of 2.88s and it was statistically insignificant ($p> 0.05$).

The corneal staining was evaluated immediately after removal of contact lenses at the end of the 3 month study. Fluorescein bands were applied after prior wetting with saline, in the inferior bulbar conjunctiva. The slit lamp evaluation was done using cobalt blue filter.

For grading the corneal staining we used the scale CCLRU modified by adding half units (0.5) in order to increase sensitivity. We achieved an overall corneal staining score and also we analyzed separately for 5 corneal staining areas: superior, inferior, nasal, temporal and central.

Regarding global values for corneal staining with fluorescein, they were between 0 and 3 for both eyes, with a mean and standard deviation of 0.50 ± 0.53. Overall staining distribution skewed to 0, but still 30% of participants experienced a corneal staining ≥ 1.

Contact lens wearers with corneal staining ≥ 1 were still asymptomatic and during the study the participants did not have any ocular inflammation or infection, during the 3 months of evaluation. It knows that fluorescein can destroy normal epithelial cells, which is why this result reinforces the idea of periodic evaluation of corneal staining to prevent possible inflammation / infection that occurs with an injured epithelium.

Using the variation analysis, we compared the sum of the degree of staining for the two eyes in the 5 areas and found a statistically significant difference between them ($p = 0.0001$). Thus, we found that the upper and lower zones have a different degree of staining from central areas, temporal and nasal.

The results of this study do correlate with the results of other studies that have shown that upper and lower regions of cornea captures more fluorescein than others in different circumstances. Korb and Korb defined the corneal staining in the upper lid as "staining of the eyelid margin" suggesting that upper eyelid closing force causes a deficiency of the tear film in the area, leading to the staining. They also defined the term "staining of eyelid closure" for staining of the lower lid, associated with blinking and dryness of the lower part of the cornea. Guillon et al. suggested that an increase in corneal staining may be associated with a lower line of the tear film instability observed in the lower eyelid margin.

All silicone-hydrogel contact lenses affects the ocular surface, corneal homeostasis is slow, smooth interactions occur between the surface of the eye and contact lens material and the tear film structure and its physiology is altered. Many of these effects are amplified by wearing during sleep, when the eye is in a pro-inflammatory status, is more sensitive to hypoxia induced by contact lenses and have closer interaction with palpebral conjunctiva, but is fully reversible when waking, in the absence of pathological situations.

Silicone-hydrogel lenses combine the benefits of soft hydrogel lenses with high oxygen transmissibility, giving wearers more flexibility in wearing and longer wearing period, with remarkable clinical benefits.

Many of lenses available today, as we have seen in the study, are providing optimal flow of oxygen reducing the hypoxic stress and having a significantly smaller effect on corneal homeostasis. However, extended wear silicone-hydrogel lenses may have a potential irreversible damage to the cornea, especially those wearers needed higher level of oxygen than average and those with large refractive errors, which are fitted in thicker lenses and thus a lower oxygen transmissibility.

Short-term effects of silicone-hydrogel lenses on tear film are insignificant, but we must take into account any individual variations. Future studies will need to assess the wider impact of silicone-hydrogel lenses on tear film, for longer periods of time and to elucidate individual differences that influence success in fitting and wearing modality.

In the questionnaire applied to the study participants, the subjective assessment revealed that many of the contact lens wearers, even of silicone-hydrogel have some degree of discomfort during wear (only 16% of carriers do not show discomfort during wear and 78% of them have discomfort rare and very rare). Rate of secretion and tear film stability, especially related to the aqueous phase and time

of tear film break TBUT are lower in contact lens wearers and this decrease tear film volume is involved in discomfort and intolerance contact lens wearers.

In our study we obtained an average value of NI-BUT of 8.04s to silicone-hydrogel contact lens wearers evaluated at the end of the study and compared to the baseline of 11.04s we found no statistically significant variation of NI-BUT.

The major challenge in contact lens fitting is to create a contact lens which interacts with the ocular surface as a healthy biocompatible cornea. From observations of this study originates that silicone-hydrogel lenses today if properly fitted, patients selected appropriately and compliant wearing regimen, replacement and care, we can achieve a high degree of adaptability and tolerance of this type of optical correction and therapeutic means also.

As in the literature, we found significant correlations between corneal thicknesses measured at the end of 3 months between the 3 groups of silicone-hydrogel contact lens users.

It was noted that the degree of conjunctival hyperemia by statistical analysis of the results of average conjunctival hyperemia, we obtained a statistically significant change from baseline and the degree of hyperemia assessed at one month of wear.

To improve the biocompatibility of these materials and the ocular surface we should better understand the factors related to contact lens and those contributing to the inflammatory response and infection.

During the study we had no cases of ocular infection. Wearer's tendency is to use in extended wear these lenses and it was confirmed that hypoxia plays a minor role for eye infections and corneal infiltrates like peripheral ulcers induced by contact lenses; the major implication for this type of wear modality is the patient selection and the proper fitting.

New strategies are needed to limit the side effects caused by prolonged retention of micro-organisms on the ocular surface, which may include the incorporation of antimicrobial agents even at the lens surface or structure.

Solutions are no longer left aside, because there is an increasing interest in the maintenance of compatibility between different systems available and new silicone-hydrogel materials, this point is actually an opportunity to develop a solution to improve tear film of the contact lens surface.

Larger modulus of silicone-hydrogel lenses compared with those of hydrogel could lead to new designs to modulate the exchange of tears and reduce mechanical interaction between the lens and ocular surface.

With all these improvements in terms of surface and silicone-hydrogel lens material, the trend currently is to silicone-hydrogel lenses disposable, which are intended to reduce or even eliminate remaining issues still under discussion of silicon-hydrogel lenses - microbial keratitis, ocular discomfort and dryness.

New challenges and perspectives emerged from progress in performance of these lenses by avoiding hypoxia. Silicone-hydrogel lenses have begun to be used for cultivation and stem cell transplantation in cases of epithelial decompensation and studied special types of contact lenses for ophthalmology (used as extended release drug reservoir or support for microchips, for the blind) and other medical fields (sensor glucose monitoring and other biological parameters), it is recommended continuous training of practitioners on the latest releases in the field.

Nowadays there are studies for discovering new technical options for avoiding infectious complications (inhibition of microbial adhesion, silver sterilization) enabling their widespread use, with minimal risks.

Since the introduction of silicone-hydrogel material, the use of contact lenses helps to broaden therapeutic opportunities and improving the quality of life for patients of all ages, so study the clinical effects of new products should continue permanently.

Annex 1 - Protocol of initial examination of the patient

Sheet No: Date:
Examine patients with contact lenses
Name: .....
Date of Birth: ..... Sex: M F
Address: .....

PATIENT HISTORY
Wear contact lenses?
□ yes
□ no
□ yes, but I do not harbor
(why not wear contact lenses:)
.....

MEDICAL HISTORY

Sinusitis Allergies Pregnancy Diabetes dry eye thyroid imbalance

MEDICATIONS USED

Diuretics, antihistamines contraceptives Tranquilizers Other (specify)

EYE EXAMS WITHOUT LENS

A.V. uncorrected OD OS AO

Sfero-cylindrical refraction and A.V. / keratometry

OD			
OS			

	K1	K2@
OD		
OS		

Topography: yes ☐ no ☐ **Number/date……**

Pachymetry OD OS

NI-BUT

OD			
OS			

Remarks:

……
……
……

Eye exams with contact lenses

	Manufacturer	Material	Dioptria	BC	Diam.	VA	VAAO
OD							
OS							

Lens care solution

Period of wear:

1 day 3 days 1 week 2 weeks 1 month 3 months 6months

Time of wear:

DW (12h / day)	EW (6 nights)	EW (30 nights)

Lens fitting

Mobility **Foto nr.....**	**OD**	**OS**
1. Adecvat		
2. **Excesiv** (>0,6mm)		
3. **Insuficien**t (<0.2mm)		
4. Aderenta		

Remarks:

Centration **Foto nr:.....**	**OD**	**OS**
. **Excelent** (Centrat)		
. **Buna** (Usoara descentrare , fara expunere corneeana)		
. **Medie** (Descentrare, expunere corneeana intermitenta)		
. **Slaba**(Acoperire corneeana incompleta si/sau ridicarea marginii)		

Annex 2 - Protocol for review of the patient

Name:

A.V. C.C. **OD** **OS** **BE**

Wearing period:

1 day	3 days	1 week	2 weeks	1 month

Wearing duration:

12 hours per day	6 nights	30 nights

Lens fitting

Centration **Numar poza.....**	**OD**	**OS**
5. Excelent (centrat)		
6. (usoara descentrare, fara expunere corneeana)		
7. **Satisfacator** (descentrare,expunere corneeana intermitenta)		
8. Nesatisfacator (acoperire corneeana incompleta si/sau ridicarea marginii)		

Mobility **Numar poza.....**	**OD**	**OS**
5. Adecvata		
6. **Excesiva** (>0,6mm)		
7. **Insuficienta** (<0.2mm)		
8. Aderenta		

Remarks:

.....

Lens depositions **Numar poza.....**	**OD**	**OS**
Gradul 0: absent		
Gradul 1: 1 – 25%		
Gradul 2: 25 – 50%		
Gradul 3: 50 – 75%		
Gradul 4: 75 – 100%		

Remarks:

.....

Topography YES ☐ NO ☐ Number / Date .....

Keratometry

	K1	K2@
OD		
OS		

Pachymetry OD ☐ **OS** ☐

NI-BUT

OD			
OS			

Remarks:

Slit lamp examination

Fluorescein test (zoneleCCLRU) Numar poza:	**OD**	**OS**
A1 (central)		
A2 (nazal)		
A3 (temporal)		
A4(superior)		
A5 (inferior)		

Fluorescein test (Profunzime) Numar poza:	**OD**	**OS**
Grade 0: absent		
Grade 1: implicare epiteliala superficiala		
Grade 2: stralucire stromala prezenta in 30 sec		
Grade 3: stralucire stromala prezenta imediat		
Grade 4: difuza stralucire stromala prezenta imediat		

Fluorescein test (Tipul) Numar poza:	**OD**	**OS**
Grade 0: absent		
Grade 1: micropunctate		
Grade 2: macropunctate		
Grade 3: coalescent macropunctate		
Grade 4: patch		
Fluorescein test (extindere in fiecare zona) Numar poza:	**OD**	**OS**
Gradul 0: absent		
Gradul1: 1-25%		
Gradul 2: 25-50%		
Gradul 3: 50-75%		
Gradul 4: 75-100%		

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